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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

CROUCH, DEBORAH

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,514	CHENG, LINZHAO	
	Examiner	Art Unit	
	Deborah Crouch	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 and 34-64 is/are pending in the application.
- 4a) Of the above claim(s) 34-51 and 57-64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 and 52-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 May 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Applicant's arguments filed January 30, 2009 have been fully considered but they are not persuasive. The amendment has been entered. 1-30 and 34-64 are pending. Claims 34-51 and 57-64 have been withdrawn from consideration as to a non-elected invention. Claims 1-30 and 52-56 are examined herein.

The rejection made in the office action mailed September 30, 2008 of claim 55 under 35 U.S.C. 112, second paragraph, is withdrawn because of amendments to the claim.

The rejection made in the office action mailed September 20, 2008 of claims 10-14, 17-19, 22-25 under 35 U.S.C. § 102(b) over Bongso is withdrawn because of amendments to the claims

The rejection made in the office action mailed September 20, 2008 of claims 31-33 are rejected under 35 U.S.C. 102(b) over Thomson is withdrawn because of amendments to the claims.

The rejection made in the office action mailed September 20, 2008 of claims 17, 26, 27, 29 and 30 under 35 U.S.C. § 103 over Xu and Lim is withdraw because of applicant's arguments.

The rejection made in the office action mailed September 20, 2008 of claims 1, 4, 15, 17 and 20 under 35 U.S.C. § 103 over Xu and McIntosh is withdraw because of applicant's arguments.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Rejections under 35 U.S.C. § 102 or 102/103

Claims 1-9 remain, and claims 18 and 25 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bongso et al. (1994) Human Reproduction, Vol. 9, pages 2110-2117 for reasons set forth in the office action mailed September 30, 2009.

In reference to claims 1-9 and 25, Bongso teaches isolated hES cells (page 2112, col. 1, parag. 1). All hES cells required, as an inherent property, either a feeder cell layer or feeder cell conditioned media. The claims do not require the presence of the feeder cells, only that the hES cells depend on them for growth. In a side by side

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comparison, a patentable distinction could not be discerned between the claimed hES cells and those of Bongso. Claim 18 states "a culture of undifferentiated pluripotential hES cells prepared by .." This claim is a culture of hES cells expanded as in claim 17; Claim 18 is not the expanded population of claim 18. Thus, Bongso anticipates the claimed invention. In the alternative, as the hES cells of the claims and those of Bongso are not patentably distinct, any differences are obvious differences.

Applicant argues the invention claimed is based on the discovery that adult human cells can be used as feeder cells for growing continuous cultures of undifferentiated pluripotent hES cells. Applicant argues hES cells passaged using the disclosed method have maintained a diploid karyotype and have remained in an undifferentiated state after continuous culture and many passages. Applicant argues Bongso is improper as the limitations of dependent on adult human bone marrow of human fibroblasts from breast skin feeder cells and are depending on these feeder cells for maintenance in culture in an undifferentiated state for 4 or more passages. Applicant argues the hES cells of Bongso did not remain in the undifferentiated state through multiple passages as presently required by the claims. These arguments are not persuasive.

Amended claim 1 reads:

Isolated undifferentiated pluripotential hES cells, wherein the hES cells exhibit dependence on adult human feeder cells or an hES cell-maintaining product of the adult human feeder cells, for maintenance in culture in an undifferentiated state for 4 or more passages, wherein the adult human feeder cells comprise human bone marrow cells or human fibroblasts from breast skin.

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The wherein clause is not given patentable weight as the language does not alter the structure of the hES cell from hES cells known in the art at the time of filing. Thus the claim is being examined as "isolated undifferentiated pluripotential hES cells."

Applicant appears to believe a structural difference has occurred to the hES cells of the claims based on the disclosed culture conditions. However, there is no evidence to support such a theory in the present record. Further, there is no evidence that Bongso's cells grown under the same conditions would not have also been dependent on adult feeder cells and grow continuously in the undifferentiated state for more than 4 passages while maintaining correct ploidy. Should applicant have any such evidence of a structural difference, such should be supplied in the form of a declaration under 37 § CFR 1.132.

Thus, while applicant may have discovered a new method for culturing hES cells, there is no reason to believe the cells themselves are different.

Claims 52, 54 and 55 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by over Xu et al., Nature Biotech, October 2001, pages 971-974.

Xu teaches a culture of hES cells grown in media supplemented with conditioned media prepared from TERT immortalized human foreskin fibroblasts (page 971, col. 2, parag. 1, lines 2-11). Xu teaches a method of subculturing by indication of passage 32 (page 972, Figure 1). Xu further teaches a method of obtaining hES cells comprising culturing hES cells in BJ5ta, an immortalized fibroblast line, conditioned media, and isolation of hES cells (page 971, col. 2, parag. 2 and page 972, fig. 1). hES cells

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inherently express SSEA-4, Oct-4, alkaline phosphatase and do not express SSEA-1.

Thus, Xu clearly anticipates the claimed invention.

Applicant argues the claims are directed to cultures of undifferentiated pluripotent hES cells or culture methods that require adult human feeder cells or an hES cell-maintaining product where the feeder cells are human bone marrow cells or human breast skin fibroblasts. Applicant argues Xu provides methods of feeder-free growth of hES cells on extracellular matrices in presence of conditioned media produced from various cell lines, including fibroblast cell lines. Applicant argues Xu does not require the particular feeder cell lines of the claimed invention.

Claims 53, 54 and 55 lack a recitation of bone marrow cells or human breast skin fibroblasts. Thus, applicant is arguing limitations not in the claims. Further, the conditioned media of Xu is “an ES cell-maintaining product.”

Claims 10-16 and 52-56 rejected under 35 U.S.C. 102(e) as being clearly anticipated by PGPub 20050037488 (Mitalipov).

Mitalipov teaches a culture of hES cells on human bone marrow stromal cells and the growth of hES cells by culturing the culture (parag. [0050], [0051] and [0146]-[0156]). The BMSC's are adult feeder cells producing an ES cell-maintaining product of the supportive adult human feeder cells. Further, Mitalipov teaches the production of conditioned media from the BMSC feeder cells and the culture of hES cells in the conditioned media (parag. [0202]). The media of Mitalipov's co-culture would contain both the feeder cells and the product. It is inherent that a portion of the BMSCs would

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be dying and non-supportive, while other BMSCs in the culture would be supportive.

Thus Mitalipov clearly anticipates the claimed invention.

Applicant argues Mitalipov is silent with regard to the use of human breast skin fibroblasts. This argument is not persuasive.

Note claim 17 is no longer part of the rejection.

Rejections under 35 U.S.C. § 103

Claims 10-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. PgPub 2005003748 (Mitalipov) in view of WO00/029001 published May 25, 2000 (McIntosh).

Mitalipov teaches a culture of hES cells on immortalized human skin fibroblasts and method of obtaining an expanded population of undifferentiated pluripotential hES cells comprising culturing the culture (parag. [0050], [0051] and [0146]-[0156]). The fibroblasts are adult feeder cells producing an ES cell-maintaining product of the supportive adult human feeder cells. Mitalipov also teaches the feeder cells can be used to produce conditioned media (parag. [0202]). Mitalipov teaches isolating hES cells so cultured for pluripotency markers (parag. [0155]). further, Mitalipov teaches subculturing hES cells on the fibroblast feeder cells (parag. [0154], lines 6-9).

McIntosh teaches fibroblast cell line 1087sk, ATCC CRL-2104 (page 11, lines 20-22). McIntosh further teaches the media from culturing the 1087sk cells was used to prepare conditioned media (page 13, lines 3-7).

Thus, at the time of the instant invention, it would have been obvious to prepare a culture of hES cells with CCD-1087sk adult human fibroblasts from breast, culture the

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culture, subculture the culture and isolate hES cells from the culture in view of Mitalipov teaching the propagation of hES cells on skin fibroblast feeder cells and McIntosh teaching CCD-1087sk human adult fibroblasts. The artisan would have known at the time of filing to obtain CCD-1087sk cells from the ATCC. The claims require growth on CCD-1087sk feeder cells. The claimed invention is a known method modified by an element from a known and predictable method.

Claims 17, 26, 27, 29 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 2005003748 (Mitalipov) in view of U.S. Patent 6,921,632 issued July 26, 2005 (Lim).

Mitalipov teaches a culture of hES cells on immortalized human skin fibroblasts and method of obtaining an expanded population of undifferentiated pluripotential hES cells comprising culturing the culture (parag. [0050], [0051] and [0146]-[0156]). The fibroblasts are adult feeder cells producing an ES cell-maintaining product of the supportive adult human feeder cells. Mitalipov also teaches the feeder cells can be used to produce conditioned media (parag. [0202]). Mitalipov teaches isolating hES cells so cultured for pluripotency markers (parag. [0155]). further, Mitalipov teaches subculturing hES cells on the fibroblast feeder cells (parag. [0154], lines 6-9).

Lim teaches the cryopreservation of hES cells in media and a cryopreservative such that the hES cells remain viable upon thawing (col. 16, lines 44-61). Lim also teaches subculture of hES cells (col. 14, lines 60-67). While Lim does not teach freezing hES cells prior to subculture, it was well known and practiced within the art at the time of filing, to freeze cell samples throughout their establishment. The idea is if

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samples are available through the stages of establishing a culture, the cells can be replaced if contaminated or otherwise lost.

Therefore, at the time of filing, it would have been obvious to the ordinary artisan to freeze aliquots or hES cells cultured in human fibroblast conditioned media as taught by Mitalipov using the cryopreservation method of Lim.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch/
Primary Examiner, Art Unit 1632

May 7, 2009